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EXAMINER	
GOON, SCARLETT Y	

ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,695	KUMAZAWA ET AL.	
	Examiner	Art Unit	
	SCARLETT GOON	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-56* is/are pending in the application.

4a) Of the above claim(s) *27,28 and 43-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-42 and 49-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *27-56* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7 August 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed 28 August 2008 in which claims 55 and 56 were newly added is acknowledged. Claims 55 and 56 find support on p. 4 and 5 of the instant specification.

Claims 27-56 are pending in the instant application.

Priority

This application is a National Stage entry of PCT/JP05/03234 filed on 21 February 2005 and claims priority to Japan foreign application 2004-043481 filed on 19 February 2004. A certified copy of the foreign priority document in Japanese has been received. No English translation has been received.

Information Disclosure Statement

The information disclosure statement (IDS) dated 7 August 2006 complies with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609, unless otherwise noted. Accordingly, it has been placed in the application file and the information therein has been considered as to the merits.

Reference AN was not considered because a copy of the document was not provided to the Office.

Election/Restrictions

Applicant's election with traverse of Group VI, claims 49 and 50, drawn to a method of inhibiting viral activity, in the reply filed on 28 August 2008 is acknowledged. The traversal is on the ground(s) that the Examiner did not sufficiently show a lack of unity because the "common technical feature is not simply the structure represented by formula (1) because the substituents must also be taken into account". This is not found persuasive because several of the substituents include many variables, and thus would not constitute as a common technical feature. Those substituents that did not include variables, namely, the acidic group of formula (1), the C-2 hydroxyl group, and the invariable portion of formula (1-1) are disclosed in the structure disclosed by Wiese *et al.* and therefore, destroys the technical feature of the instantly claimed invention.

Although the Applicant's argument was not persuasive, upon further consideration of the Restriction Requirement dated 28 July 2008, the restriction requirement is modified as follows: Group II, claims 29-42 and 51-54 will be rejoined with Group VI, claims 49 and 50. Newly added claims 55 and 56 belong to the invention of Group VI and will be examined with claims 29-42 and 49-54 herein.

Applicants further elect, with traverse, in the reply dated 28 September 2008, the compound of formula (3), wherein R^6 is H and R^5 is represented by R^{52}, as the singly disclosed species. The traversal is on the ground(s) that each and every compound of chemical formula (1) is not patentably distinct from each other. This argument is found persuasive. Therefore, as Applicants have elected the compound of formula (3), wherein R^6 is H and R^5 is represented by R^{52}, as the singly disclosed species, the

compound of formula (3), wherein R^6 is H and R^5 is represented by R^{58} will also be searched as these two compounds are not patentably distinct from each other.

The requirement as it currently stands is deemed proper and is therefore made FINAL.

Claims 27-28 and 43-48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 29-42 and 49-56 will be examined herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 49, 53 and 54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 49 recites the limitation "the cell according to claim 27" in lines 2 and 3. There is insufficient antecedent basis for this limitation in the claim. Claim 27 discloses a cell activator and not a cell.

The recitation "NO production" in claims 53 and 54 render the claims herein indefinite. Abbreviations can be interpreted differently depending on the context and the art. Thus, it is unclear whether "NO" refers to nitric oxide or whether it just means lack of production, or whether it is an abbreviation for something else. To render the claim

definite, it is suggested that Applicants spell out what they intend to claim, rather than use abbreviations. If Applicants intend to use an abbreviation in the claims, it is suggested that the words first be spelled out in the first claim where it is used before using abbreviations in subsequent claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-42 and 49-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of activating NKT cells, NK cells and dendritic cells, accelerating the production of cytokines, accelerating nitric oxide production, and inhibiting viral activity in cytomegalovirus (such as herpes virus) by administering particular glycolipids of formula (1), does not reasonably provide enablement for activating NKT cells, NK cells and dendritic cells, accelerating the production of cytokines, and inhibiting viral activity in any viral infection by administering any compound of formula (1). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2)

the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

All of the *Wands* factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The rejected invention is drawn to a method of activating NKT cell, activating NK cell, accelerating IL-4, accelerating IFN-γ, activating dendritic cell, accelerating IL-12, accelerating IL-10, accelerating IL-6, accelerating nitric oxide production, and inhibiting any viral activity, which comprises administering a compound of formula (1) to a mammal.

Relative skill of those in the art: The relative skill of those in the art is high.

Breadth of claims: The claims are extremely broad in that they encompass literally the inhibition of any viral activity with any compound of formula (1), and the acceleration of cytokines and activation of NKT cell, NK cell and dendritic cell with any compound of formula (1).

State of the prior art/Predictability or unpredictability of the art: The skilled artisan would view that it is highly unlikely that one could successfully inhibit any viral activity with any compound of formula (1). Similarly, the skilled artisan would view that it is highly unlikely that one could successfully activate NKT cell, NK cell, accelerate cytokines, accelerate dendritic cells and accelerate nitric oxide production using any compound of formula (1). At the very minimum, particularly long alkyl or alkenyl chains

of R^3 and R^4 would result in issues of solubility and hydrophobicity/hydrophilicity, thereby rendering them poor drugs. With respect to R^2, receptors recognizing antigenic molecules can be fairly specific with regards to their carbohydrate recognition sites, due to the high variability in their stereocenters. Thus, it is unlikely that any combination of the monosaccharides disclosed would suffice in inhibiting viral infection.

Additionally, the skilled artisan would view that it is highly unlikely that one could inhibit any and all viral activity with a compound of formula (1). As discussed in the Merck Manual (PTO-892, Ref. U), there are many different types of viral infections. The most common are those of the nose, throat, and upper airways (p. 1, last paragraph). However, there are also viruses that infect the nervous system and others that infect the skin (p. 2, paragraph 2). Thus, there are many different actions in which a virus can infect an individual. Current antiviral drugs work by either interfering with the replication of viruses or by strengthening the immune system (p. 2, subheading "Treatment", paragraphs 1 and 2). Thus, the mode of action of the drug will determine which virus the antiviral will be effective against.

Furthermore, there are many animal models available for testing of different viral infections. The applicants used a mouse virus model that mimics cytomegalovirus in humans. One of skill in the art would not view effectiveness based on one type of virus model to translate to effectiveness in other types of virus models. As shown in the listing of antiviral drugs and their common uses, as disclosed by the Merck Manual (PTO-892, page 1, Ref. U), there are currently no antiviral drugs that are effective across the spectrum against a variety of viral infections. As such, one of ordinary skill in

the art would be very skeptical to translate the positive results from one viral type to all other viral infections.

Amount of guidance/Existence of working examples: The specification only discloses the antiviral effects of four glycolipids (GSL-1, GSL-2, GSL-6 and GSL-7) in a mouse cytomegalovirus model. For activation of NKT cells, only glycolipids GSL-1, GSL-2, GSL-6 and GSL-7 were tested for activity. For acceleration of IFN-γ and activation of dendritic cells, compounds GSL-1 through GSL-13 were tested. For However, these compounds do not cover the full scope of the compounds represented in the claims by the structure of formula (1). Similarly, for the activation of NK cells and the induction/acceleration of cytokines and nitric oxide, only a handful of GSLs were tested. There are **no** working examples present which show that the methods claimed can be effected by all of the compounds of formula (1). Additionally, there are **no** working examples present to indicate that the compounds tested are effective against any virus other than cytomegalovirus.

Lack of a working example is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.

Thus, the specification fails to provide clear and convincing evidence in sufficient support of the use of the claimed methods for activating NKT cells, NK cells and dendritic cells, accelerating the production of cytokines, accelerating nitric oxide production, and inhibiting viral activity in cytomegalovirus (herpes virus) by administering particular glycolipids of formula (1), as recited in the instant claims.

Genetech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors as discussed above, e.g., the amount of guidance provided, the predictability of the art and the lack of working examples, to practice the claimed invention herein, a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Section [0001]

Claims 29-34, 39-42, 49-52, 55 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over journal publication by Kakimi *et al.* (PTO-892, Ref. V), in view of journal publication by Wu *et al.* (IDS dated 7 August 2006) and journal publication by Wiese *et al.* (of record).

Kakimi *et al.* teach that natural killer T (NKT) cell activation by α-galactosylceramide (α-GalCer) inhibits hepatitis B virus replication *in vivo*. The antiviral effect of α-GalCer is rapid and specific, and is associated with the induction of IFN-γ and IFN-α/β in the liver (p. 927, column 1, subheading "Discussion"). Since the induction of IFN-γ and IFN-α/β as well as the inhibition of HBV replication occur before a significant number of inflammatory cells are recruited into the organ, it is likely that these cytokines are produced by cells that reside in the liver, specifically NKT cells that are known to produce IFN-γ very rapidly in response to α-GalCer and NK cells that are promptly activated by NKT cells and enhance induction of IFN-γ production (p. 927, column 2, bridging paragraph). Based on the results of their study, Kakimi *et al.*

conclude that α-GalCer inhibits HBV replication by directly activating NKT cells and by secondarily activating NK cells to secrete antiviral cytokines in the liver (p. 921, abstract).

Kakimi *et al.* do not explicitly teach activation of NKT cells, NK cells and inhibition of HBV by the compound of formula (3) wherein R^6 is H and R^{51} is as shown in instant claim 28.

Wu *et al.* teach bacterial glycolipids and analogs as antigens for CD1d-restricted NKT cells. α-GalCer, a lipid found in marine sponge, when bound to CD1d, stimulates rapid Th1 (such as IFN-γ) and Th2 (such as IL-4) cytokine production by NKT cells in mice and human (p. 1351, column 1, bridging paragraph; Figure 1). The glycolipids shown in figure 2 were also tested for their ability to stimulate mouse and human natural killer T (NKT) cells. Compounds 1 and 2 represent *Sphingomonas* bacterial glycolipids that are structurally similar to α-GalCer, but differ mainly in the acidic group present on the carbohydrate (p. 1352, column 1, first incomplete paragraph). These structures may be more physiologically relevant as natural ligands for CD1d-mediated NKT cell activation because they originate from bacteria (p. 1352, column 1, first incomplete paragraph), as compared to marine sponge. Stimulation of the NKT cell line by the glycolipid compounds resulted in significant IFN-γ and IL-4 secretion, when compared to the negative control (p. 1355, paragraph 2, last paragraph). In addition to stimulating NKT cells, flow cytometric analyses indicated that the receptor of NKT cells also bind to the various glycolipid antigen structures (p. 1356, column 1, first complete paragraph). Since the *Sphingomonas* glycolipids were reactive to the same population of human

NKT cells as α-GalCer, Wu *et al.* concluded that this indicates that bacterium-derived antigens are also able to activate NKT cells (p. 1356, column 2, subheading "Conclusion", paragraph 2). Furthermore, they were able to demonstrate responses to the *Sphingomonas* compounds *in vivo*, and mice deficient for NKT cells have a reduced ability to clear bacteria from the liver (p. 1356, column 2, subheading "Conclusion", paragraph 1).

Wiese *et al.* teach the characterization of some physiochemical properties of the monosaccharide-type fraction of glycosphingolipids from the outer leaflet of the Gram-negative species *Sphingomonas paucimobilis.* Its structure is shown in Figure 1, indicating it has two variants for the R group (p. 322).

It is noted that the references do not explicitly teach a method of accelerating IL-10 and IL-6 production which comprises administering the cell activator to a mammal. However, Wu *et al.* explicitly teach that α-GalCer, when bound to CD1d, stimulates rapid Th1 and Th2 cytokine production by NKT cells in mice and human (p. 1351, column 1, bridging paragraph; Figure 1). As evidenced by Trinchieri *et al.* (PTO-892, Ref. W), Th2 cytokine production includes IL-4, IL-5, IL-6 and IL-10 (p. 123, column 1, first paragraph).

As such, it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Kakimi *et al.*, concerning the inhibition of hepatitis B replication by the activation of NKT cells by α-GalCer, with the teachings of Wu *et al.*, regarding the effect of various glycolipids, including *Sphingomonas* bacterial glycolipids, in activating NKT cells and cytokine production, with the teachings of Weise

et al., regarding the physiochemical properties of glycolipids from the bacteria *Sphingomonas paucimobilis*. Since Kakimi *et al.* teach that α-GalCer can activate NKT cells and NK cells, thereby inhibiting hepatitis B replication, and Wu *et al.* teach that α-GalCer analogs wherein lipids varying in chain lengths still have significant activities toward NKT cell activation and that the *Sphingomonas* bacterial glycolipids carrying the acidic group may be more physiologically relevant as natural ligands for CD1d-mediated NKT cell activation because they originate from bacteria and not marine sponge (origination of α-GalCer), and Weise *et al.* teach various structures of glycolipids from the bacteria *Sphingomonas paucimobilis*, one would have been motivated to combine the teachings in order to receive the expected benefit, as suggested by Wu *et al.*, that the structures from *Sphingomonas paucimobilis* may be more physiologically relevant as natural ligands for CD1d-mediated NKT cell activation because they originate from bacteria (p. 1352, column 1). Thus, as viruses are infectious agents are more similar to bacteria than marine sponge, these compounds may also be more physiologically relevant in inhibiting hepatitis B replication. Furthermore, since Wu *et al.* indicated that glycolipids with varying chain lengths still have significant activities toward NKT cell activation, one of ordinary skill in the art would know that this structural component of the glycolipid does not play a significant role in NKT cell activation.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Section [0002]

Claims 29-40, 51 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over journal publication by Kitamura *et al.* (PTO-892, Ref. X), in view of journal publication by Wu *et al.* (IDS dated 7 August 2006) and journal publication by Wiese *et al.* (of record).

Kitamura *et al.* teach the NKT cell ligand, α-GalCer, demonstrates its immunopotentiating effect by inducing IL-12 production by dendritic cells and IL-12 receptor expression on NKT cells. As shown in Figure 3, Kitamura *et al.* demonstrated that α-GalCer upregulates IL-12 R expression *in vivo* and this upregulation is blocked by mAbs against Il-12 or IFN-γ (p. 1125, column 2, last paragraph). Based on the results of their experiments, Kitamura *et al.* speculate that the following series of events is induced upon culture of α-GalCer with dendritic cells and NKT cells: (a) α-GalCer first binds to CD1d molecules on dendritic cells; (b) NKT cells recognize α-GalCer-bound dendritic cells via their TCRs and also interact with dendritic cells via CD40/CD40L; (c) during this interaction, the dendritic cells produce IL-12; (d) the endogenously produced IL-12 stimulates IFN-γ production by NKT cells; and (e) IFN-γ produced by NKT cells upregulates IL-12R on NKT cells in an autocrine manner.

Kitamura *et al.* do not explicitly teach activation of NKT cells, acceleration of cytokines and activation of dendritic cells by the compound of formula (3) wherein R^6 is H and R^{51} is as shown in instant claim 28.

The teachings of Wu *et al.* and Wiese *et al.* were as described above in section [0001] of the claim rejections under 35 USC § 103.

As such, it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Kitamura *et al.*, concerning the immunopotentiating effect of α-GalCer in inducing IL-12 production by dendritic cells, with the teachings of Wu *et al.*, regarding the effect of various glycolipids, including *Sphingomonas* bacterial glycolipids, in activating NKT cells and cytokine production, with the teachings of Weise *et al.*, regarding the physiochemical properties of glycolipids from the bacteria *Sphingomonas paucimobilis*. Since Kitamura *et al.* teach that α-GalCer upregulates IL-12 production by activating dendritic cells, and Wu *et al.* teach that α-GalCer analogs wherein lipids varying in chain lengths still have significant activities toward NKT cell activation and that the *Sphingomonas* bacterial glycolipids carrying the acidic group may be more physiologically relevant as natural ligands for CD1d-mediated NKT cell activation because they originate from bacteria and not marine sponge (origination of α-GalCer), and Weise *et al.* teach various structures of glycolipids from the bacteria *Sphingomonas paucimobilis*, one would have been motivated to combine the teachings in order to receive the expected benefit, as suggested by Wu *et al.*, that the structures from *Sphingomonas paucimobilis* may be more physiologically relevant as natural ligands for CD1d-mediated NKT cell activation because they originate from bacteria (p. 1352, column 1). Since Wu *et al.* indicated that glycolipids with varying chain lengths still have significant activities toward NKT cell activation, one of ordinary skill in the art would know that this structural component of the glycolipid does not play a significant role in NKT cell activation, and thus can use a large array of glycolipids for NKT cell and NK cell activation and cytokine acceleration.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Section [0003]

Claims 53 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over journal publication by Tay *et al.* (PTO-892, page 2, Ref. U), in view of journal publication by Kakimi *et al.* (PTO-892, Ref. V), journal publication by Wu *et al.* (IDS dated 7 August 2006), and journal publication by Wiese *et al.* (of record).

Tay *et al.* teach that the antiviral effector mechanisms by which NK cells control murine cytomegalovirus (MCMV) infection in the liver are abrogated by *in vivo* administration of L-NMMA, a competitive inhibitor of NOS (nitric oxide synthase). Treating mice with L-NNMA enhanced MCMV titers in the liver (p. 272, bridging paragraph; p. 273, column 2, first full paragraph). This data adds to the evidence that one of the ways IFN-γ can exert its antiviral actions is through the induction of NOS to produce nitric oxide (p. 273, column 2, first full paragraph).

Tay *et al.* do not explicitly teach a method wherein NO production is accelerated by the compound of formula (3) wherein R^6 is H and R^{51} is as shown in instant claim 28.

The teachings of Kakimi *et al.*, Wu *et al.*, and Wiese *et al.* were as described above in section [0001] of the claim rejections under 35 USC § 103.

As such, it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Tay *et al.*, concerning the induction of NO production by NK cells and IFN-γ in murine cytomegalovirus infection, Kakimi *et al.*,

regarding the inhibition of hepatitis B replication (cytomegalovirus) by the activation of NKT cells and NK cells by α-GalCer, with the teachings of Wu *et al.*, regarding the effect of various glycolipids, including bacterial glycolipids, in activating NKT cells and cytokine production, with the teachings of Weise *et al.*, regarding the physiochemical properties of glycolipids from the bacteria *Sphingomonas paucimobilis*. Since Kakimi *et al.* teach that α-GalCer can activate NKT cells and NK cells, thereby inhibiting hepatitis B replication, Tay *et al.* teach that NO production is effected by IFN-γ, and Wu *et al.* teach that α-GalCer analogs wherein lipids varying in chain lengths still have significant activities toward NKT cell activation and that the *Sphingomonas* bacterial glycolipids carrying the acidic group may be more physiologically relevant as natural ligands for CD1d-mediated NKT cell activation because they originate from bacteria and not marine sponge (origination of α-GalCer), and Weise *et al.* teach various structures of glycolipids from the bacteria *Sphingomonas paucimobilis*, one would have been motivated to combine the teachings in order to receive the expected benefit, as suggested by Wu *et al.*, that the structures from *Sphingomonas paucimobilis* may be more physiologically relevant as natural ligands for CD1d-mediated NKT cell activation because they originate from bacteria (p. 1352, column 1). Since Wu *et al.* indicated that glycolipids with varying chain lengths still have significant activities toward NKT cell activation, one of ordinary skill in the art would know that this structural component of the glycolipid does not play a significant role in NKT cell activation.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SCARLETT GOON whose telephone number is 571-270-5241. The examiner can normally be reached on Mon - Thu 7:00 am - 4 pm and every other Fri 7:00 am - 12 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang, Ph.D./
Supervisory Patent Examiner, Art Unit 1623

/SCARLETT GOON/
Examiner
Art Unit 1623